# THE INFLUENCE OF VARIATIONS IN TEMPERATURE AND BLOOD-PRESSURE ON THE PERFORMANCE OF THE ISOLATED MAMMALIAN HEART.

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THE isolation of the heart after the method of Newell Martin[1] possessed certain advantages over other methods. The heart is supplied with blood properly oxygenated by the lungs and it pumps the blood against a measured resistance, and thus can be made to work under conditions closely approximating to the normal. The chief drawback to the method was that a comparatively large amount of blood was needed, necessitating the bleeding of a number of animals or the use of calves' blood obtained from a slaughter-house. The toxic influence of such blood on the dog's heart is evident in many of Martin's records.

By the use of the mercury resistance as described by Jerusalem and Starling[2], the method is greatly simplified, the amount of blood required is much less, and it is possible to keep the heart nourished with the blood of the one animal. The one serious objection to this method is the contact of the blood with mercury. As the blood passes over and through the mercury enough is taken up to have a deleterious effect. The lung capillaries suffer first, and after a somewhat variable period pulmonary œdema usually terminates the experiment. We have therefore substituted for the mercury a more satisfactory resistance and at the same time retained the many obvious advantages of the method.

*Description of method.* By this method it is possible to determine the output of the left ventricle under approximately normal conditions, and to vary at will the arterial resistance, the venous pressure, the filling of the heart, or the temperature of the blood supply to the heart. The arrangement of the apparatus is shown in the figure (Fig. 1).

Artificial respiration being maintained the chest is opened under an anæsthetic. The arteries coming from the arch of the aorta—in the cat, the innominate and the left subclavian—are then ligatured, thus cutting off the whole blood supply to the brain, so that the anæsthetic can be discontinued. The azygos vein is ligatured. Cannulæ are placed in the innominate artery and the superior vena cava. The cannulæ are filled beforehand with a solution of hirudin in normal salt solution, so as to prevent clotting of the blood during the experiment.

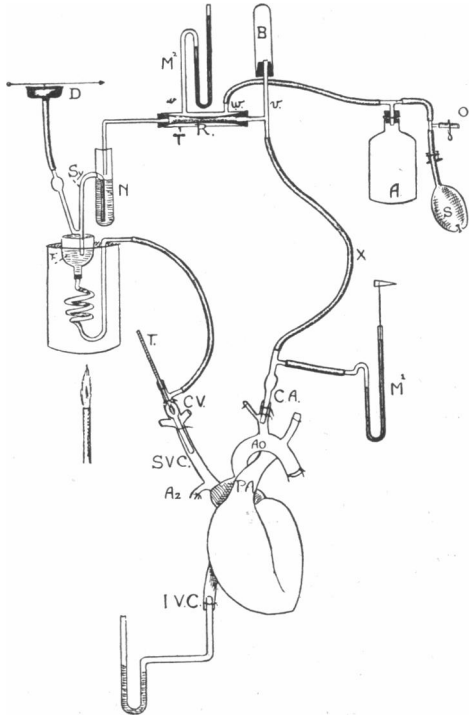


Fig. 1.

The descending aorta is closed by a ligature and the only path left for the blood is by the ascending aorta and the cannula CA in the innominate artery. The arterial cannula communicates by a T-tube with a mercurial manometer to record the mean arterial pressure and passes to another T-tube v, one limb of which projects into a test-tube B. The air in this test-tube will be compressed with a rise of pressure and will serve as a driving force for the blood through the resistance. It thus takes the part of the resilient arterial wall. The

other limb of the T-tube passes to the resistance R. This consists of a thin-walled rubber tube (*e.g.* a rubber finger-stall) which passes through a wide glass tube T, provided with two lateral tubulures ww. One of these is connected with a mercurial manometer and the other with an air reservoir A, into which air can be pumped by the elastic bellows S. When air is injected into T the tube R is compressed and will remain so until the pressure of the blood within it is equal or superior to the pressure in the air surrounding it. It is thus possible to vary at will the resistance to the outflow of the blood from the arterial side. From the peripheral end of R the blood passes at a low pressure and is collected in a vessel N, which is provided with a siphon and can be made of such dimensions that the blood is siphoned off as soon as 10, 20 or 30 c.c. have collected in the vessel. A lateral branch on the siphon tube leads on a rubber tube to a tambour D. Every time that siphonage occurs there is a change of pressure within the tambour which is registered by the lever of the tambour. The siphon discharges the blood into a reservoir F, which is kept immersed in a vessel of water maintained at any desired temperature by some source of heat. From the spiral below F an india-rubber tube leads to a cannula CV, which is placed in the superior vena cava, all the branches of which have been tied. This cannula is provided with a thermometer to show the temperature of the blood supplied to the heart. A tube placed in the inferior vena cava and connected with a water manometer shows the pressure in the right auricle. On the recording surface we thus have a record of the arterial pressure, of the output of the whole system, as recorded by the tambour, and of the pressure within the right auricle. In cases where it was desired to record the volume of the heart this was effected by means of a glass cardiometer and a float recorder, as described in the paper already quoted(2).

I. *The effects of changes in the arterial resistance on the frequency and output of the heart and on the arterial and venous pressures.*

(*a*) *Effect on the frequency of contraction.* Changes in arterial resistance, with accompanying changes in pressure in the coronary vessels and changes in tension of the ventricular walls, were found to be without effect on the frequency of the heart contractions. To pressures varying between 20 mm. and 200 mm. Hg the heart

responded with unaltered rhythm and rate, provided the temperature of the circulating blood remained constant. In one instance an apparent alteration in rate was found to be due to the fact that the heart was beating with alternating weak and strong contractions. On raising the pressure this irregularity disappeared to reappear when the pressure was again lowered. Our observations thus confirm those of Martin and others. The various alterations in the cardiac rhythm which, in the intact animal, accompany vaso-motor and other activities, must be due to factors other than the direct action of the pressure changes on the heart.

(*b*) *Effect on the output of the left ventricle.* If we start with a low resistance, the arterial pressure being 20—30 mm. Hg, and raise the resistance gradually to a maximum, the output at first increases with

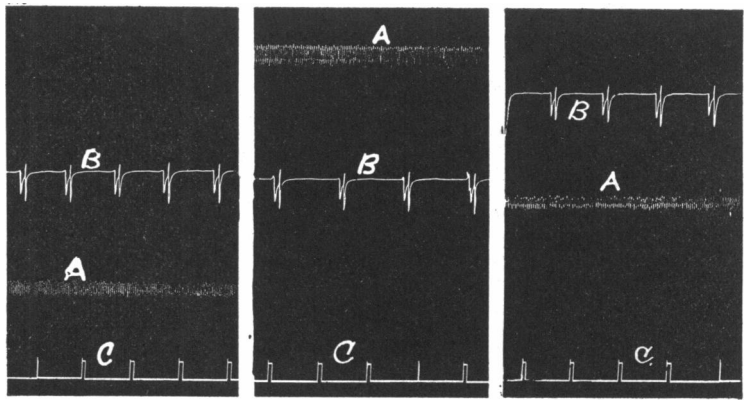


Fig. 2. A = arterial pressure. B = output = 12·5 c.c. C = zero-pressure line and time = 10 secs. Temp. = 35° C.

increase of pressure until a maximum is reached. This output is maintained until a point is reached at which the resistance becomes too great for the heart to overcome. The output then falls off rapidly (Fig. 2).

The pressure range at which the greatest output was maintained was, in cats, between 102 and 150 in one experiment, from 84 to 154 in another, from 80 to 120 in a third. In one experiment on the dog's heart the range was between 54 and 108. The point of highest pressure at which we get maximum output maintained varies with the species and age of the animal and with the condition of the heart at

the time of observation. In general it seems to lie near the average blood-pressure found normally in the animal. It is higher in the cat than in the dog, in agreement with the higher blood-pressure normally occurring in the cat. It is lower in younger and smaller animals than in older ones of the same species.

It may be of interest to note that the maximum output (left ventricle) of the average full-grown cat was not far from 1 c.c. per heart beat. Cardiometer records show that the volume, both systolic and diastolic, of the ventricles varies with the arterial pressure, gradually increasing as the pressure rises and diminishing again

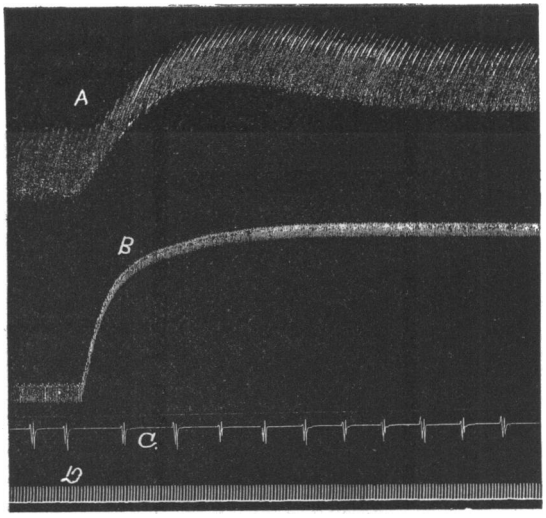


Fig. 3. Sudden increase of arterial resistance. Temp. = 34° C. A = ventricular volume. B = arterial pressure. C = output of left ventricle. D = seconds and zero-pressure line.

when it is lowered. When the pressure is raised suddenly the ventricle first dilates, then diminishes in size as its tone improves (Fig. 3).

When a pressure which the heart is unable to overcome is reached, the dilatation then becomes extreme and the heart fails to recover its tone unless the pressure is rapidly lowered.

The initial improvement in efficiency with increasing arterial resistance seems to be mainly due to the increased pressure and consequent improvement of the coronary circulation. The stimulating action of increased tension within the ventricle also may be a factor.

In a few of the experiments we have calculated the work of the left ventricle from the formula $w = v.p.$, $v$ being the amount of blood pumped out during a given time and $p$ being the arterial blood-pressure recorded at the time.

The following is the result from Exp. 1. Cat. Weight of heart = 15·5 gms.

| Arterial pressure mm. Hg | Output c.c. per min. | Work per minute |
|---|---|---|
| 40 | 116 | 62·64 gm. meters. |
| 70 | 112 | 105·61 ,, |
| 90 | 126 | 153·46 ,, |
| **130** | 98·2 | **229·78** ,, |
| 140 | 61 | 115·29 ,, |
| 150 | 44·3 | 89·70 ,, |
| 156 | 37·5 | 78·97 ,, |

In another experiment with a larger heart (weight 19·5 grams) from an older animal, the work amounted to 267·53 gram meters, at an arterial pressure of 180 mm. Hg, the highest pressure studied. This was probably not far from the real maximum, as at this pressure the output was beginning to diminish.

The results of five typical experiments in which the arterial resistance was varied while the venous pressure and inflow remained constant, are shown in the following table:

Exp. 1. Cat, 3·9 kilos. Weight of heart 15·5 gms.

| | Temp. of art. blood | Heart beats in 20 secs. | Art. B.-P. Hg | Venous pressure cm. | Output of heart c.c. per min. | Output of heart per min. c.c. per gm. |
|---|---|---|---|---|---|---|
| Art. resistance low | 35·0 | 58 | 44 | 2·8—6 | 125·12 | 6·30 |
| Art. resistance raised | 35·0 | 58 | 102 | 2·2—6 | 138·00 | 7·07 |
| Art. resistance raised | 34·8 | 57 | 118 | 2·2—6 | 138·00 | 7·07 |
| Art. resistance raised | 34·8 | 57 | 176 | 7·4—10·8 | 112·6 | 5·80 |

Exp. 2. Cat, 3·9 kilos. Heart 15·5 gms.

| | Temp. of venous blood | | | | | |
|---|---|---|---|---|---|---|
| Art. resistance low | 37·4 | 50 | 40 | 2·2 | 116·00 | 7·50 |
| Art. resistance raised | 37·4 | 49 | 70 | 2·4 | 112·00 | 7·29 |
| ,, ,, | 37·4 | 51 | 90 | 3·5 | 126·00 | 7·80 |
| ,, ,, | 37·4 | 48 | 130 | 7·0 | 98·20 | 6·34 |
| ,, ,, | 36·7 | 47 | 140 | 6·2 | 61·00 | 3·94 |
| ,, ,, | 36·7 | 47 | 150 | 8·0 | 44·30 | 2·86 |
| ,, ,, | — | 46 | 156 | 13·0 | 37·50 | 2·45 |

Exp. 3. Cat. Height of venous reservoir 6 cm.

| | Temp. of art. blood | Heart beats in 20 secs. | Arterial B.-P. Hg | Output c.c. per minute |
|---|---|---|---|---|
| Art. resistance low | 35 | 51 | 38 | 73·2 |
| ,, ,, raised | 35 | 51 | 132 | 52·5 |
| ,, ,, lowered | 35 | 51 | 50 | 69·5 |

Exp. 4. Small dog. Height of venous reservoir 10 cm.

| | Temp. of art. blood | Heart beats in 20 secs. | Arterial B.-P. Hg. | Output c.c. per min. |
|---|---|---|---|---|
| Art. resistance low | 36 | 32 | 54 | 174·0 |
| ,, ,, raised | 36 | 32 | 108 | 127·0 |
| ,, ,, ,, | 36 | 32 | 136 | 55·6 |
| Exp. 5. Cat. Venous reservoir 6 cm. | | | | |
| Art. resistance low | 36·5 | 76 | 60 | 61·0 |
| ,, ,, raised | 36·5 | 76 | 126 | 61·0 |

## II. *The influence of alterations on the venous inflow and the venous pressure on the rate and work of the heart.*

Changes of venous inflow produced by varying the height of the venous reservoir have surprisingly little effect on the different phases of cardiac activity, with the exception of the output. We were unable to produce alterations in frequency by even extreme changes in the venous pressure. As the venous reservoir is raised and the output of the heart increased, the arterial pressure as measured near

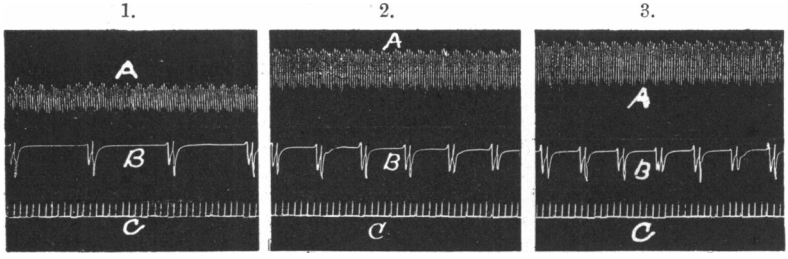


Fig. 4. Effect of changes in venous inflow. A = arterial pressure. B = ventricular output. C = zero-pressure and seconds.

1. Venous reservoir 6 cm. Venous pressure 2·8—3·2 cm.
2. ,, ,, 16 ,, ,, ,, 3—6 ,,
3. ,, ,, 26 ,, ,, ,, 3—6 ,,

the heart naturally rises, although the arterial resistance is unaltered, since the greater quantity of blood has to be forced through the same resistance. The rise of pressure under these circumstances is only inconsiderable since a small rise of pressure serves to dilate the rubber tube of the arterial resistance and so allow the passage of a greater quantity of blood. The output was the one factor markedly affected (Fig. 4). Up to the limit of its capacity, the isolated heart will pump out from the venous side all the blood it receives and it does this without any change in the frequency of its contractions. Accordingly the venous pressure does not rise at first as we raise the reservoir, or

rises only slightly. When we reach the point of maximum output the venous pressure rises rapidly. If the high venous pressure is maintained, pulmonary œdema always appears. For this reason high venous pressures are studied with difficulty. Unless they are produced momentarily and then lowered the consequent œdema soon brings the experiment to an end.

If therefore we have to obtain the maximal work out of a heart it is necessary always to measure the pressure in the right auricle by means of a cannula introduced into the inferior vena cava. The venous reservoir is then raised until this pressure just begins to rise. With an active heart considerable changes in the height of the venous

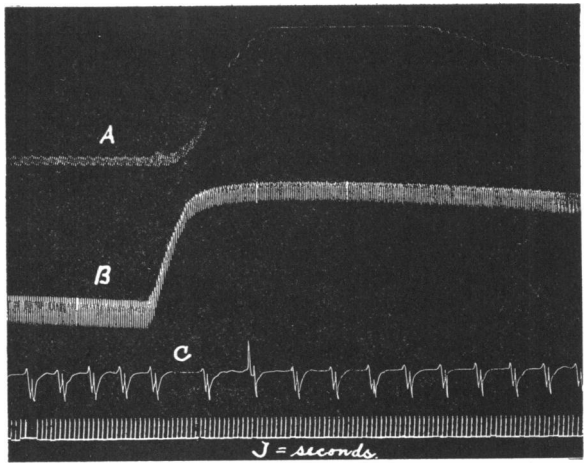


Fig. 5. Sudden rise of arterial pressure. A = venous pressure changes. B = arterial pressure. C = output of left ventricle. S = seconds and zero-pressure line.

reservoir may be made before they are reflected in the height of the venous manometer. As the heart begins to fail in the course of a long experiment the first sign of its failure is seen in the venous manometer, and if the experiment is to be prolonged it is necessary to lower the venous reservoir until the venous manometer returns to its previous height. If attention be paid to this point we can be certain of having a heart which has been working at the maximum of its physiological efficiency throughout the whole of the experiment. In the same way a temporary insufficiency of the heart is at once reflected on the venous pressure. In Fig. 5 a sudden rise of arterial pressure produced temporary dilatation and inefficiency of the ventricles, and a

corresponding rise of venous pressure and diminished output. As the heart gradually improved under the influence of the increased circulation through the coronary arteries, the output increased and the venous pressure gradually came back to its previous level. The beginning of this return of venous pressure is shown in the figure. These points are brought out in the following records of experiments.

Exp. 6. Cat. 4·1 kilos.

| | Temp. of art. blood | Heart beats in 20 secs. | Art. B.-P. Hg | Venous pressure cm. $H_2O$ | Output of heart c.c. per min. | Output of heart per min. c.c. per gm. |
|---|---|---|---|---|---|---|
| Venous reservoir low = 6 cm. ... | 34 | 55 | 46 | 3·8—5·0 | 61·0 | 3·10 |
| Venous reservoir raised = 16 cm. | 34 | 55 | 56 | 4·0—7·2 | 112·2 | 5·70 |
| Venous reservoir raised = 26 cm. | 34 | 56 | 60 | 4·2—7·2 | 138·0 | 7·04 |
| Exp. 7. Cat. | | | | | | |
| Venous reservoir low = 6 cm. ... | 33·0 | 48 | 116 | 3·0—4·6 | 45·9 | — |
| Venous reservoir raised = 16 cm. | 35·4 | 64 | 164 | 3·0—6·0 | 126·5 | — |
| Venous reservoir raised = 26 cm. | 34·5 | 57 | 176 | 7·4—10·0 | 112·0 | — |
| Exp. 8. Cat. | | | | | | |
| Venous reservoir low = 6 cm. ... | 33·0 | 56 | 134 | — | 56·1 | — |
| Venous reservoir raised = 16 cm. | 33·0 | 56 | 154 | — | 112·2 | — |

## III. *The influence of variations in temperature on the heart.*

Under most conditions the frequency of contraction of the isolated heart remains unaltered. To change of temperature it is extraordinarily sensitive. Although there are a considerable number of observations on the influence of temperature on the isolated heart, few of them were under conditions which so closely approach the normal. We have therefore studied the effects of change of temperature, especially through that range within which the heart is able to maintain an efficient circulation. The results are shown in the accompanying tables[1].

[1] Readings were taken at half degree intervals. To save space every alternate reading has been omitted from the printed Table.

*Influence of temperature on dog's heart.*

| | Temp. venous blood | Heart beats in 20 secs. | Arterial pressure | Output |
|---|---|---|---|---|
| Cooling. Venous reservoir 10 cm. throughout. | 30·0 | 28 | 110 | 174·0 |
| | 29·5 | 27 | 110 | 174·0 |
| | 28·0 | 23 | 108 | — |
| | 27·5 | 23 | 108 | 156·2 |
| | 26·5 | 21 | 100 | 139·0 |
| Began warming ... ... | 27·0 | 22 | 100 | 156·2 |
| | 28·0 | 25 | 98 | 174·0 |
| | 29·0 | 28 | 98 | 174·0 |
| | 30·0 | 31 | 98 | 174·0 |
| | 31·0 | 34 | 98 | 174·0 |
| | 32·0 | 36 | 106 | 174·0 |
| | 33·0 | 39 | 106 | 174·0 |
| | 34·0 | 41 | 106 | 174·0 |
| | 35·0 | 44 | 106 | 174·0 |
| | 36·0 | 46 | 104 | 191·2 |
| | 37·0 | 49 | 102 | 191·2 |
| | 38·0 | 52 | 100 | 191·2 |
| | 39·0 | 53 | 98 | 191·2 |
| | 40·0 | 54 | 98 | 191·2 |
| | 41·0 | 55 | 98 | 191·2 |
| | 42·0 | 55 | 96 | 191·2 |
| | 43·0 | 55 | 98 | 191·2 |
| | 44·0 | 52 | 98 | 191·2 |
| | 45·0 | 29 | 96 | — |
| Heart very irregular ... ... | 46·0 | — | 94 | — |
| Heart stopped ... ... | 47·6 | — | — | — |

*Influence of temperature on cat's heart.*

| | Temp. venous blood | Heart beats in 20 secs. | Arterial pressure | Venous pressure | Output c.c. per min. |
|---|---|---|---|---|---|
| | 30·0 | 41 | 72 | 3·0—4·0 | 104·8 |
| | 29·5 | 39 | 72 | 3·0—4·0 | 104·8 |
| | 28·5 | 34 | 72 | 3·0—4·0 | 104·0 |
| | 27·5 | 31 | 72 | 3·0—4·0 | 100·7 |
| | 27·0 | 29 | 72 | 3·0—4·0 | 100·7 |
| | 26·5 | 27 | 72 | 3·0—4·0 | 100·7 |
| Heart suddenly began to dilate ... | 26·0 | — | — | — | — |
| | 25·5 | 25 | 72 | 8·5—10·5 | 56·0 |
| Art. resist. and ven. reserv. lowered | 27·0 | 27 | 38 | 3·5—5·0 | 83·1 |
| Art. resist. raised ... ... | 28·0 | 29 | 66 | 3·5—5·5 | 83·1 |
| Venous reservoir raised ... | 29·0 | 31 | 68 | 3·0—5·5 | 104·8 |
| | 30·0 | 34 | 68 | 3·0—5·5 | 104·8 |
| | 31·0 | 38 | 68 | 2·4—4·4 | 104·8 |
| | 32·0 | 41 | 68 | 2·4—4·4 | 104·8 |
| | 33·0 | 43 | 68 | 2·4—4·4 | 104·8 |
| | 34·0 | 48 | 68 | 2·0—4·0 | 112·0 |
| | 35·0 | 51 | 68 | 2·0—4·0 | 112·0 |
| | 36·0 | 53 | 68 | 2·0—4·0 | 112·0 |
| | 37·0 | 57 | 68 | 2·0—4·0 | 112·0 |
| | 38·0 | 59 | 68 | 2·0—4·0 | 112·0 |
| | 39·0 | 61 | 68 | 2·0—4·0 | 112·0 |
| | 40·0 | 65 | 68 | 2·0—4·0 | 112·0 |
| | 41·0 | 65 | 68 | 2·0—4·0 | 112·0 |
| | 42·0 | 67 | 66 | 2·2—3·2 | 112·0 |
| | 43·0 | 67 | 64 | 2·2—3·2 | 104·8 |
| Irregular ... ... ... | 44·0 | 65 | 64 | 3·0—4·0 | 104·8 |
| Cooled down to 23. | | | | | |

The minimal temperature at which the mammalian heart can beat against what may be called an average resistance varies between 23° and 26° C. As the heart is gradually cooled, when the critical temperature is reached it suddenly dilates, the output diminishes rapidly, and unless the arterial resistance is relaxed and the blood warmed quickly the heart ceases to beat, often going into fibrillary contraction.

In the case of a heart embarrassed by a cardiometer the critical temperature was 26° C. (Fig. 6). In other cases it was as low as 23° C. When the arterial pressure is relaxed as the heart is cooled, it may go on beating more and more slowly and fully until a much lower point is reached.

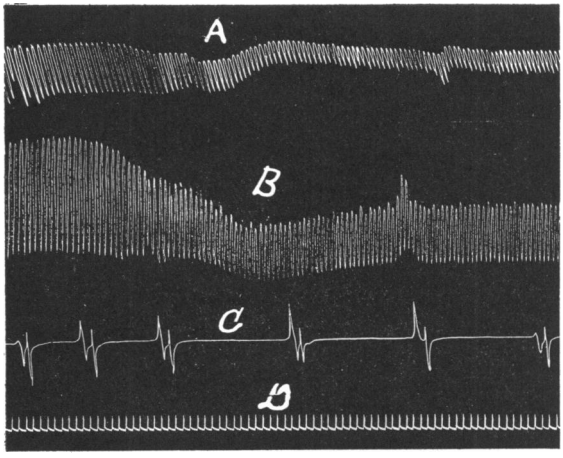


Fig. 6. Effect of cooling. Sudden failure of the output and arterial pressure at 26° C. A = ventricular volume. B = arterial pressure. C = ventricular output. D = zero-pressure line and seconds.

The maximal temperature lies above 40°. The heart may continue beating for some time at a temperature of 45° to 46° but irregularities in rhythm begin to appear at temperatures above 40°.

Throughout that range, which we may call the physiological range, *i.e.*, within the limits in which it can do its work efficiently, each increase or decrease produces a uniform change in rate whether the temperature be high or low. If such effects are plotted as a curve (Fig. 7) they form a straight line, the variations from it being such as arise unavoidably from the method of experiment.

It seems therefore misleading to speak of a temperature coefficient for the heart. Though we can express the relation between the heart rates at any two temperatures by multiplying the lower rate by a factor, this factor will vary continuously with the temperature. By picking out two points on the curve we might obtain the coefficient of 2 for a rise of 10°, in agreement with Snyder(3), but this coefficient would not apply to any other two points. Throughout the physiological range the increment of rate is arithmetically proportional to the increment of temperature.

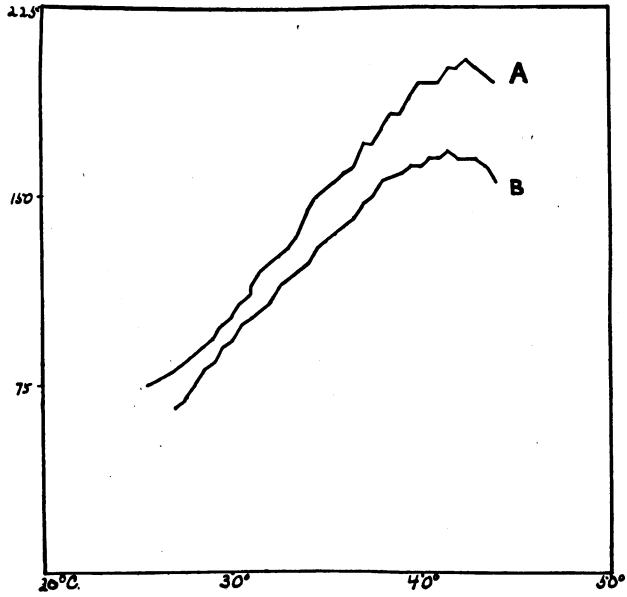


Fig. 7.

Only when the heart is beginning to fail as a result of exposure to too high or too low a temperature do we obtain any deviation from the strict proportionality between the temperature and the rate of the heart beat.

Of late years a number of experiments have been made on various physical processes with a view to determine whether these are 'physical' or 'chemical' in nature. If a process is found to have a heat coefficient for ten degrees of about 2, the fact is regarded as an indication that the process is essentially chemical in nature. The same line of argument would lead us to the conclusion that the influence of temperature on the heart is mainly physical; but surely the whole argument is somewhat futile. The increase in pressure of a volume of gas under the influence of temperature is proportional to the absolute temperature, and we call it a physical process. The change in the conductivity of a solution of an electrolyte depends on any increase in ionisation of the solute, on the increased molecular energy or the velocity of translation of the ions, and on changes in

the viscosity of the solution. When we deal with a reaction ordinarily spoken of as chemical, we are dealing with a similar complex of phenomena. Even in such cases it is difficult to say where a physical process ends and a chemical process begins,—in fact there is no line of demarcation. When a chemical process has been analysed it will have been brought into the domain of physics. Though at the present time a division between chemical and physical phenomena may often be convenient, though not logical, it is surely out of place when we are dealing with the nature of the phenomena occurring in the complex systems of surfaces which make up the living cell.

In a recent paper Snyder sums up the results of a number of researches on the influence of temperature on physiological processes. Among certain curves that he gives we find one for the cat's heart. This, like ours, is practically a straight line. He gives the temperature coefficient as 2·3, but the coefficient has to be varied continuously with the temperature, which seems rather a forced interpretation of a direct proportionality found between heart rate and temperature.

It will be noted from the tables quoted that temperature has very little influence on the output of the ventricle; at whatever rate the heart was beating the output remained approximately the same throughout a wide range of temperature, *i.e.*, between about 33° and 40° C. A diminution in output per minute was the first sign that the fall or rise of temperature was exceeding physiological limits.

## IV. *The effect of extrinsic nerves on the isolated heart.*

Whatever may be its controlling mechanism, the heart isolated as in the method described remains susceptible to both inhibitory and accelerator impulses through the cardiac nerves. As indicated in the following table, the effects of stimulating the sympathetic and the vagus nerves were tested at a low and at a moderately high temperature. The rate of the isolated heart beat at any temperature must be

*Isolated heart of dog. Effect of stimulation of cardiac nerves.*

| | Temp. venous blood | Heart beats 20 secs. | Arterial pressure | Output c.c. per min. |
|---|---|---|---|---|
| Before stimulation ... | 35·7 | 30 | 74 | 112·0 |
| Stimulation of sympathetic | 35·7 | 71 | 90 | 126·0 |
| 1 min. later ... ... | 36·5 | 61 | 76 | 126·0 |
| Before stimulation ... | 36·5 | 54 | 76 | 112·0 |
| Stimulation of left vagus ... | 36·5 | 17 | — | — |
| After ... ... ... | — | 54 | — | 126·0 |
| Later ... ... ... | — | 51 | — | 112·0 |
| Stimulation of sympathetic | — | 64 | — | 139·0 |
| Cooled ... ... ... | 28·8 | 36 | 98 | 108·7 |
| Stimulation of left vagus ... | 28·8 | 28 | 86—100 | 98·2 |
| After ... ... ... | 28·8 | 38 | 100 | 112·0 |
| Stimulation of sympathetic | 28·8 | 44 | 100 | 112·0 |

considered as a mean. Whatever may be the processes concerned they are susceptible both to retardation and augmentation by the influence of nerve impulses. The influence of the accelerator nerves on the heart is shown in Fig. 8. We did not succeed in maintaining the irritability of the cardiac nerves in the cat's heart when isolated in this manner sufficiently long to test the efforts of their excitation.

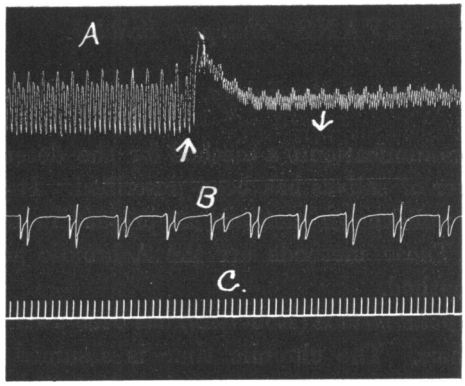


Fig. 8. Stimulation of sympathetic nerves. A = arterial pressure. B = ventricular output. C = seconds and zero-pressure line.

## SUMMARY.

(1) The rate of the isolated heart fed with normal oxygenated blood is determined entirely by temperature, being unaltered by changes within wide limits either of arterial resistance or venous pressures.

(2) The rate of heart beat varies directly as the temperature, the curve showing its relation to temperature being a straight line.

(3) Within wide limits, the output of the heart is independent of arterial resistance and of temperature.

(4) Up to a certain point the output of the heart is proportional to the venous inflow. When this point is exceeded, the venous pressure rises, and œdema of the lungs supervenes.

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